REMARKS

These amendments simply correct typographical errors and add no new matter to the specification.

The amendment made on page 20, lines 14-15, completes the title of the book cited. The author, first half of the title, publisher and year of publication were all cited correctly, and from this information the book could easily be found.

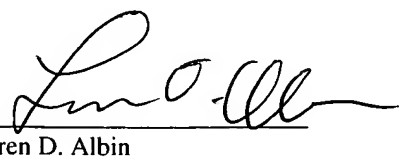
The amendments made to the article title on page 28, line 11, add a quotation mark to the beginning of the title and replace "in" with a colon. Neither of these errors would prevent someone from easily finding this article.

The amendment made on page 28, line 21, places an umlaut over the "o" in the first named author's last name. This error would not prevent someone from easily finding this article.

The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

CERTIFICATE UNDER 37 C.F.R. 1.8:

The undersigned hereby certifies that this paper is being deposited in the United States Postal Service, as first class mail, in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on this 1st day of March, 2002.



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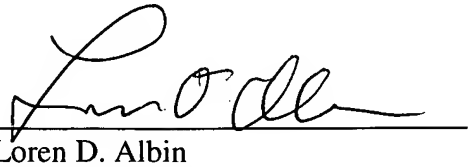
By: 

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APPENDIX A - SPECIFICATION/CLAIM AMENDMENTS INCLUDING NOTATIONS TO INDICATE CHANGES MADE
Serial No.: 10/027,227
Docket No.: 00481.CN1
Filed: December 21, 2001
For: CRYSTALLIZATION AND STRUCTURE DETERMINATION OF GLYCOSYLATED HUMAN BETA SECRETASE, AN ENZYME IMPLICATED IN ALZHEIMER'S DISEASE

Amendments to the following are indicated by underlining what has been added and bracketing what has been deleted. Additionally, all amendments have been shaded.

In the Specification

At page 20, line 1-16

Thus, this method involves generating a preliminary model of a molecule or molecular complex whose structure coordinates are unknown, by orienting and positioning the relevant portion of human beta secretase or the human beta secretase/inhibitor complex within the unit cell of the crystal of the unknown molecule or molecular complex so as best to account for the observed x-ray diffraction pattern of the crystal of the molecule or molecular complex whose structure is unknown. Phases can then be calculated from this model and combined with the observed x-ray diffraction pattern amplitudes to generate an electron density map of the structure whose coordinates are unknown. This, in turn, can be subjected to any well-known model building and structure refinement techniques to provide a final, accurate structure of the unknown crystallized molecule or molecular complex (Lattman, "Use of the Rotation and Translation Functions," in Meth. Enzymol. 115, pp. 55-77 (1985); M.G. Rossman, ed., ["The Molecular Replacement Method," Int. Sci. Rev. Ser. No. 13] The Molecular Replacement Method - A Collection of Papers on the Use of Non-Crystallographic Symmetry, Intl. Sci. Rev. Ser. No. 13, Gordon & Breach, New York (1972)).

At page 28, lines 9-17

Useful programs to aid one of skill in the art in connecting the individual chemical entities or fragments include, without limitation, CAVEAT (Bartlett et al., in "Molecular Recognition: [in] Chemical and Biological Problems," Special Publ., Royal Chem. Soc., 78:182-96 (1989); Lauri et al., J. Comput. Aided Mol. Des. 8:51-66 (1994); available from the University of California, Berkeley, CA); 3D database systems such as ISIS (available from MDL Information Systems, San Leandro, CA; reviewed in Martin, J. Med. Chem. 35:2145-54 (1992)); and HOOK (Eisen et al., Proteins: Struc., Funct., Genet. 19:199-221 (1994); available from Molecular Simulations, San Diego, CA).

At page 28, lines 18-26

Human beta secretase binding compounds may be designed "*de novo*" using either an empty binding site or optionally including some portion(s) of a known inhibitor(s). There are many *de novo* ligand design methods including, without limitation, LUDI ([Bohm]Böhm, J. Comp. Aid. Molec. Design. 6:61-78 (1992); available from Molecular Simulations Inc., San Diego, CA); LEGEND (Nishibata et al., Tetrahedron, 47:8985 (1991); available from Molecular Simulations Inc., San Diego, CA); LeapFrog (available from Tripos Associates, St. Louis, MO); and SPROUT (Gillet et al., J. Comput. Aided Mol. Design 7:127-53 (1993); available from the University of Leeds, UK).